



Oral Mucormycosis Post-COVID-19

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ABSTRACT

Mucormycosis is a deep seated systemic fungal infection. The rise in the cases of mucormycosis during COVID-19 is alarming. This review assesses different aspects to identify and treat mucormycosis. Association of COVID-19 and mucormycosis can be prevented by early diagnosis. Conservative treatment is possible if the fungal infection is detected in early stage. However, surgical methods would imply if perforation and widespread infection involving the bone is present.

Keywords: Mucormycosis, COVID-19, Early Diagnosis, Fungal disease, opportunistic infection

Introduction

The novel coronavirus 2019 or severe respiratory syndrome coronavirus 2 disease has emerged as a global pandemic. The disease ranges from mild to life threatening pneumonia with associated bacterial and fungal coinfections. Due to the associated comorbidities and immunocompromised conditions, the patients are prone to serious

opportunistic infections. There are case reports showing Post-Covid mucormycosis infection during corticosteroid therapy [1].

Fungi are eukaryotic organisms containing well defined nucleus, mitochondria, Golgi apparatus and endoplasmic reticulum. Fungi differ from other eukaryotic organisms in structural properties as the cell wall is rigid

and composed of chitin and glucan whereas the cell membrane possess ergosterol as major sterol components. These unique properties are helpful in diagnosis and treatment of fungal infection.

Fungal infections are more complex than the bacterial and viral infections. Oral mycosis/fungal infections largely comprised of opportunistic fungi. The immunosuppressed state of an individual allows for induction and development of pathogens. The oral mycosis disease ranges from superficial to deep-seated fungal infections [2-3].

Mucormycosis also known by other names such as phycomycosis or zygomyces and as black fungus among common people. Mucormycosis is a deep-seated fungal infection which presents as acute and aggressive forms. It is an acute opportunistic infection. It is caused by saprophytic fungus like *Rhizopus*, *Mucor*, *Cunninghamella*, *Rhizomucor*, *Saksenae*, *Apophysomyces* or *Lichtheimia* which are found in soil, bread moulds, rotten fruits and vegetables and animal manure. It causes systemic involvement and can be fatal if left untreated [4].

Pathogenesis

Mucormycosis affects individuals with low immunity or in immunocompromised state such as Diabetics, organ transplant, malignancies, long term steroids, etc. *Rhizopus* and *Mucor* are chiefly responsible for most cases. The organism can be cultured from the swabs obtained from oral cavity, nasal cavity, throat and stools of an individual. Spores of the fungi germinate to form hyphae upon entering the host. (Hyphae are thread like tubes containing fungal cytoplasm and its organelle and mass of hyphae is known as mycelium). These hyphae are the prime reason behind the development of signs and symptoms of this disease [5-6].

Clinical Features

Oral mucormycosis usually occurs in rhinomaxillary region, paranasal sinuses or nasal areas. It can also cause palatal necrosis and/or ulceration, intraoral draining sinuses, para-sinusal pain as a result of widespread

infection of nasal cavity or maxillary sinus. Patient exhibits facial cellulitis, blackish discoloration of skin, halitosis (bad breath), loosening of teeth, anesthesia, necrotic turbinate, nasal stuffiness with discharge, erythema of nasal mucosa, periorbital edema and orbital pain with ptosis/diplopia and fever, headache and fatigue. If left untreated, disease can spread to surrounding structures like orbit and to brain and can become life threatening. Case reports are there for oral mucormycosis involving maxilla and mandible, oroantral fistula and perforations extending to face [7-10].

Diagnosis

Perforation and necrosis of the bone are usual presentation of this disease. However, biopsy is recommended and microscopic examination is required. The histopathology based on hematoxylin and eosin microscopy shows broad (4 to 20 micron meters), non-septate hyphae with a pathognomic feature of branching of hyphae at right angle. Special stains like Periodic acid-Schiff (PAS), Gomori-Gomori methylamine silver stain confirms the presence of non-septate hyphae nature of mucormycosis. There is deep connective tissue invasion with areas of necrosis and necrotic bony trabeculae. There is inflammatory infiltrate largely comprised of poly-morph neutrophils. It can be seen invading the blood vessels. The microorganism can be cultured on SDA (Sabouraud's dextrose agar) and can be recognized by their representative patterns of carbohydrate assimilation. The microorganism should be negative for Galactomannan and Beta-Glucan test so as to exclude Aspergillosis infection. Clinical and histopathology is the gold standard for diagnosis of mucormycosis [11-16].

Management

The treatment modality depends upon the level of tissue necrosis. Liposomal Amphotericin B and Isavuconazole is the most common choice of drug for treatment. Combination of Amphotericin B and posaconazole have synergistic effects in preventing fungal hyphae germination.

Surgical debridement of tissue is required if there is bony involvement.

Mucormycosis in the aftermath of COVID-19

The novel coronavirus 2019 or severe respiratory syndrome coronavirus 2 disease ranges from mild to life threatening pneumonia with associated bacterial and fungal coinfections. Due to the associated comorbidities and immunocompromised conditions, the patients are prone to serious opportunistic infections (Refer Table 1). There are case reports showing development of mucormycosis infection during corticosteroid therapy for COVID-19. The clinical hallmark

of mucormycosis is tissue necrosis manifested as a necrotic/ulcerative lesion, eschar or black discharge in the nasal or oral cavity. Potassium hydroxide (KOH) wet mount, Calcofluor stain and fungal culture and sensitivity tests from the biopsy obtained from nasal swab were diagnostic. Liposomal Amphotericin B remains the drug of choice along with surgical debridement if required, is the treatment of mucormycosis. All physicians should be careful and mindful for the subsequent development of mucormycosis in patients with COVID-19 associated immune dysregulation and especially diabetic population.

Table 1. Points to remember about Mucormycosis

Practice points to remember				
Sign and Symptoms	Predisposing factors	What to do??	What not to do?	How to manage?
Pain and redness around eyes/nose	Uncontrolled Diabetes mellitus	Control hyperglycaemia	Do not miss sign and symptoms	Control diabetes
Fever	Immunosuppression by steroids	Use steroid judiciously	Do not hesitate to seek medical advice	Reduce steroid intake
Headache	Prolonged ICU stay	Use clean sterile water during oxygen therapy	Do not lose time to initiate treatment	Discontinue immunomodulating drugs
Shortness of breath	Co-morbidities	Use antibiotics/antifungals judiciously		Surgical debridement if needed
Altered mental status	Voriconazole therapy	Monitor blood glucose levels regularly		Maintain adequate hydration

Conclusions

Oral mycosis may vary depending upon the pathogen. However, swelling and/or invasion/ulceration or perforation of bone are the signs of Mucormycosis fungal infections. Immunocompromised patients are the risk group for Mucormycosis. Prime diagnosis can be achieved by thorough clinical examination followed by microbiological methods.

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